

CLAIMS

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- 5 1. The use of an inhibitor of the interaction of glutamate with the AMPA receptor complex and of the interaction of glutamate with the kainate receptor complex in the manufacture of a medicament for treating a demyelinating disorder.
2. The use of an inhibitor of the interaction of glutamate with the AMPA receptor complex in the manufacture of a medicament for treating a demyelinating disorder.
- 10 3. The use of an inhibitor of the interaction of glutamate with the kainate receptor complex in the manufacture of a medicament for treating a demyelinating disorder.
- 15 4. The use according to any preceding claim, wherein the demyelinating disorder is acute disseminated encephalomyelitis, acute demyelinating polyneuropathy (Guillain Barre syndrome), chronic inflammatory demyelinating polyneuropathy, multiple sclerosis, Marchifava-Bignami disease, central pontine myelinolysis, Devic syndrome, Balo disease, HIV- or HTLV-myelopathy, progressive multifocal leucoencephalopathy, or a secondary demyelinating disorder.
- 20 5. The use according to any of claims 1 to 3, wherein the secondary demyelinating disorder is CNS lupus erythematoses, polyarteritis nodosa, Sjögren syndrome, sarcoidosis or isolated cerebral vasculitis.
- 25 6. The use according to any of claims 1 to 5, wherein the inhibitor is an antagonist of the binding of glutamate to the AMPA receptor.
7. The use according to any of claims 1 to 5, wherein the inhibitor is an antagonist of the binding of glutamate to the kainate receptor.

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8. The use according to any preceding claim, wherein the inhibitor is an L-glutamate derivative, an α -amino-3-hydroxy-5-methyl-4-isoxazolepropionate derivative, arylthioxaline (42), acid amide (59), hydrazone (48), quinoline (51), quinolinone (70,78), quinoxaline (8,9,13,14,15,17,20,47,50,52,53,54,55,56),
 5 quinoxalinedione (7,11,23,43,57,58,60,61,74,77,81), triazoloquinoxalinedione (3,4,5), pyrrolylquinoxalindione (6), quinazolinone (22), quinazolinedione (35), quinoxalinone (29), phenylpyridazinoindoleone (41), indenopyrazinone (24,32,63,65,66,67,68), imidazoloquinoxalinone (12), indolo-pyrazinone (64), imidazo-pyrazinone (31,33,34,37,44,62), triazolo-pyrazinone (30), benzothiadiazine (16,36), 4-
 10 hydroxypyrrolone, pyrrolo-pyridazinone (40), phthalazine (25), quinolone (18,19), amino-alkanoic acid (1), isatine (72), phenyl-azolophthalazine, amino- or desamino-2,3-benzodiazepine (10,26,27,28,38,49,79), 2,3-benzodiazepin-4-one (21), imidazobenzodiazepine (71), β -carboline-3-carboxylic acid, alkoxy-phenyl-benzodiazepine, isoquinolinyl-carboxylic acid derivatives (75), acetyl-aminophenyl-
 15 dihydro-methyl-dioxolo-benzodiazepine, pyrimidinone (46), oxadiazol (80), isatinoxime, decahydroisoquinoline (69,73,76), piperazine derivative (2), tetramic acid derivatives (39), or a sulphamate. (The reference numbers used above correspond with the numbers used in the list of antagonists provided in the description.)
- 20 9. The use according to any of claims 1 to 7, wherein the inhibitor is L-glutamic acid diethylester, 2,3-dihydroxy-6-nitro-7-sulfamoyl-benzo(F)quinoxaline (NBQX), 6,7-dinitro-quinoxaline-2,3-dione (DNQX), 6-nitro-7-cyano-quinoxaline-2,3-dione (CNQX), 6-(1-imidazolyl)-7-nitro-quinoxaline-2,3(1H,4H)-dione (YM90K), (3RS,4aRS,6RS,8aRS)-6-(2-(1H-tetrazole-5-yl)ethyl)-decahydroiso-quinoline-3-
 25 carboxylic acid (LY293558), 9-methyl-amino-6-nitro-hexahydro-benzo(F)quinoxalinedione (PNQX), 8-methyl-5-(4-(N,N-dimethylsulphamoyl)phenyl)-6,7,8,9-tetrahydro-1H-pyrrolo[3,2h]-isoquinoline-2,3-dione-3-O-(3-hydroxybutyric acid-2-yl)oxime (NS 1209), 6,7-dichloro-2-(1H)-quinolinone-3-phosphonate (S 17625-2), and [1,2,3,4-tetrahydro-7-morpholinyl-2,3-dioxo-6-(trifluoromethyl)quinoxalin-1-
 30 yl]methyl-phosphonate (ZK200775), 1-(4-aminophenyl)-4-methyl-7,8-methylene-

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- 5 dioxo-5H-2,3-benzodiazepine (GYKI52466), (-)-1-(4-aminophenyl)-4-methyl-7,8-methylenedioxy-4,5-dihydro-3-methylcarbamoyl-2,3-benzodiazepine (GYKI53773), topiramate, 3-(2-chlorophenyl)-2-[2-[6-[(diethylamino)methyl]-2-pyridinyl]ethenyl]-6-fluoro-4(3H)-quinazolinone (CP465022) and 5-(2-[N,N-dimethylamino]oxyphenyl)-3-phenyl-1,2,4-oxadiazol (BIIR561).

10. The use according to any of claims 1 to 5, wherein the inhibitor is an AMPA receptor channel blocker.
- 10 11. The use according to any of claims 1 to 5, wherein the inhibitor is a kainate receptor channel blocker.
12. The use according to claim 10, wherein the AMPA receptor channel blocker is fluorowillardiine or Joro spider toxin.
- 15 13. The use according to claim 11, wherein the kainate receptor channel blocker is fluorowillardiine or Joro spider toxin.
- 20 14. The use according to any preceding claim wherein the inhibitor is combined with one or more of: an immunosuppressive agent (e.g. corticotrophin, a glucocorticoid, cyclophosphamide, cyclosporine, azothioprine or mitozantrone), an interferon (IFN; IFN-beta-1a e.g. Rebif and Avonex; IFN-beta-1b e.g. Betaseron and Betaferon; IFN-alpha-2a e.g. Alphaferone; IFN-alpha-2b e.g. Viraferon), a phosphodiesterase type IV inhibitor, a humanised monoclonal antibody against a
- 25 leukocyte adhesion molecule (e.g. Antegran), a synthetic polypeptide (e.g. glatiramer acetate, copolymer-1), a tissue matrix metalloproteinase (MMP) inhibitor (e.g. hydroxamic acid-based inhibitors of MMPs), or a tumour necrosis factor (TNF) inhibitor (e.g. Thalidomide or TNF-receptor immunoglobulin fusion protein).

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15. A pharmaceutical composition comprising an inhibitor as described in any of claims 1 to 14 and a pharmaceutically acceptable carrier.
- 5 16. A combined preparation of an inhibitor as described in any claims 1 to 14 and one or more of: an immunosuppressive agent (e.g. corticotrophin, a glucocorticoid, cyclophosphamide, cyclosporine, azothioprine or mitozantrone), an interferon (IFN; IFN-beta-1a e.g. Rebif and Avonex; IFN-beta-1b e.g. Betaseron and Betaferon; IFN-alpha-2a e.g. Alphaferone; IFN-alpha-2b e.g. Viraferon), a phosphodiesterase type IV inhibitor, a humanised monoclonal antibody against a leukocyte adhesion molecule
- 10 (e.g. Antegran), a synthetic polypeptide (e.g. glatiramer acetate, copolymer-1) a tissue matrix metalloproteinase (MMP) inhibitor (e.g. hydroxamic acid-based inhibitors of MMPs) or a tumour necrosis factor (TNF) inhibitor (e.g. Thalidomide or TNF-receptor immunoglobulin fusion protein)
- 15 for simultaneous, separate or sequential use in the treatment of a demyelinating disorder.
17. The invention substantially as hereinbefore described.

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